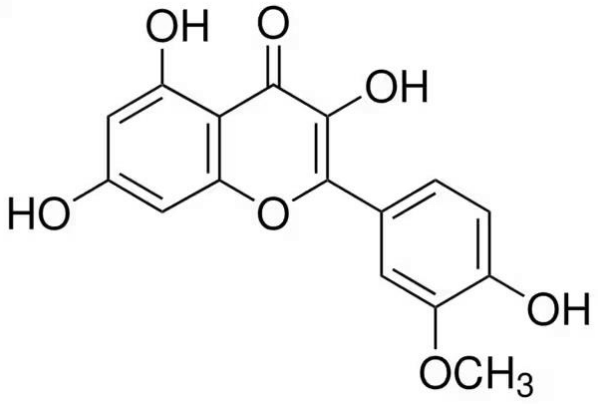


Fig. S1. The chemistry structure of isorhamnetin.

Table S1 Summary of differential metabolites in serum of HUA mice

Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MW0052448	Docosahexaenoic acid	FA	$C_{22}H_{32}O_2$	7.76	1.47	0.03	up	down
MW0121074	5-Acetylamino-6-formylamino-3-methyluracil	Heterocyclic compounds	$C_8H_{10}N_4O_4$	1.47	1.48	0.01	up	down
MEDP0437	Ergothioneine	Organic acid and Its derivatives	$C_9H_{15}N_3O_2S$	2.79	1.57	0.04	up	-
MW0109274	Pipecolic acid	Organic acid and Its derivatives	$C_6H_{11}NO_2$	1.28	1.29	0.03	up	-
MW0143662	S-methyl-5-thio-D-ribofuranose	Organic acid and Its derivatives	$C_6H_{12}O_4S$	2.89	1.52	0.02	up	-
MEDN1006	Uric acid	Organic acid and Its derivatives	$C_5H_4N_4O_3$	0.86	1.66	0.02	up	-
MEDN1476	Allantoic acid	Organic acid and Its derivatives	$C_4H_8N_4O_4$	0.88	1.65	0.03	up	-
MW0005091	4-Hydroxybenzoic acid	Organic acid and Its derivatives	$C_7H_6O_3$	2.47	1.46	0.02	up	-
MW0104792	2-Keto-3-deoxy-6-phosphogluconate	Organic acid and Its derivatives	$C_6H_{11}O_9P$	1.19	1.41	0.02	up	-
MEDP0212	N-Acetylserotonin	Tryptamines,Cholines,Pigments	$C_{12}H_{14}N_2O_2$	4.01	1.40	0.03	up	-
MW0140460	(6E)-8-oxogeranial	Aldehyde,Ketones,Esters	$C_{10}H_{14}O_2$	5.11	1.45	0.02	up	down
MW0007422	Isoproterenol	Hormones and hormone related compounds	$C_{11}H_{17}NO_3$	0.86	1.62	0.00	up	-
MW0014906	6-Keto-prostaglandin F1alpha	Hormones and hormone related compounds	$C_{20}H_{34}O_6$	5.39	1.56	0.01	up	down
MEDP1637	11-Dehydrocorticosterone	Hormones and hormone related compounds	$C_{21}H_{28}O_4$	5.38	1.56	0.01	up	-

Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MW0103557	Flavin adenine dinucleotide	Nucleotide and Its metabolites	$C_{27}H_{33}N_9O_{15}P_2$	3.30	1.62	0.00	up	down
MW0103543	Dihydroflavine-adenine dinucleotide	Nucleotide and Its metabolites	$C_{27}H_{35}N_9O_{15}P_2$	3.30	1.60	0.00	up	down
pme3174	Cytidine-5'-monophosphate	Nucleotide and Its metabolites	$C_9H_{14}N_3O_8P$	2.24	1.62	0.00	up	-
MW0125928	1-Methyl-6-oxo-1,6-dihydropyridine-3-carboxamide	Alcohol and amines	$C_7H_8N_2O_2$	1.81	1.58	0.00	up	down
MW0110911	Aminopropylcadaverine	Alcohol and amines	$C_8H_{21}N_3$	0.91	1.61	0.01	up	down
MW0118597	2-hydroxy-3,4-dihydro-2H-1,4-benzoxazin-3-one	Benzene and substituted derivatives	$C_8H_7NO_3$	3.00	1.40	0.03	up	down
MW0120692	4-Pyridoxic acid	Benzene and substituted derivatives	$C_8H_9NO_4$	1.93	1.52	0.01	up	-
MEDN0061	N-Phenylacetylglycine	Amino acid and Its metabolites	$C_{10}H_{11}NO_3$	3.58	1.51	0.02	up	-
MEDL02021	Sarcosine	Amino acid and Its metabolites	$C_3H_7NO_2$	0.83	1.42	0.04	up	-
MEDN0784	9-OxoODE	FA	$C_{18}H_{30}O_3$	8.20	1.42	0.03	up	down
MEDN0751	(±)12-HETE	FA	$C_{20}H_{32}O_3$	7.41	1.57	0.01	up	-
MEDN0785	LTB4	FA	$C_{20}H_{32}O_4$	6.19	1.65	0.00	up	down
MW0052792	Stearic acid	FA	$C_{18}H_{36}O_2$	7.84	1.48	0.03	up	-
MW0114380	(3R,4S)-2-(Phosphonooxymethyl) tetrahydrofuran-2,3,4-triol	Steroids	$C_5H_{11}O_8P$	5.93	1.66	0.02	up	-
MW0154229	(S)-2-acetamido-6-oxopimelic acid	Organic acid and Its derivatives	$C_9H_{13}NO_6$	1.37	1.49	0.02	up	-
MW0104793	2-Mercaptoethanesulfonic acid	Organic acid and Its derivatives	$C_2H_6O_3S_2$	0.63	1.58	0.02	up	-

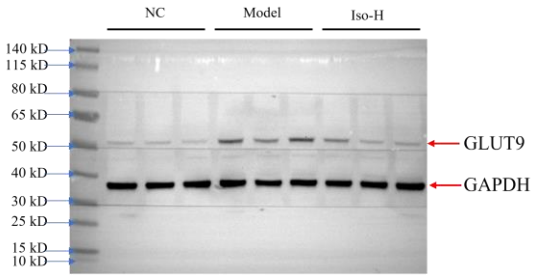
Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MW0143270	2-Hydroxy-4-oxobutane-1,2,4-tricarboxylic acid	Organic acid and Its derivatives	$C_7H_8O_8$	1.37	1.67	0.02	up	-
MEDN0622	Porphobilinogen	Organic acid and Its derivatives	$C_{10}H_{14}N_2O_4$	2.08	1.60	0.01	up	-
MW0105420	Acetylenedicarboxylic acid	Organic acid and Its derivatives	$C_4H_2O_4$	0.86	1.69	0.00	up	down
MW0114960	N-acetyl-alpha-D-glucosamine 1-phosphate	Organic acid and Its derivatives	$C_8H_{16}NO_9P$	0.79	1.65	0.01	up	-
MW0148306	D-erythro-3-methylmalic acid	Organic acid and Its derivatives	$C_5H_8O_5$	1.14	1.54	0.02	up	down
MW0011071	(R)-2,3-Dihydroxy-3-methylvalerate	Organic acid and Its derivatives	$C_6H_{12}O_4$	1.67	1.46	0.02	up	-
MW0125992	Orotic acid	Organic acid and Its derivatives	$C_5H_4N_2O_4$	0.83	1.68	0.03	up	-
MEDN0204	Pyruvic Acid	Organic acid and Its derivatives	$C_3H_4O_3$	1.36	1.56	0.01	up	-
MW0114738	Linamarin	Carbohydrates and Its metabolites	$C_{10}H_{17}NO_6$	2.26	1.61	0.01	up	-
MEDL00098	Pseudouridine	Nucleotide and Its metabolites	$C_9H_{12}N_2O_6$	0.79	1.67	0.00	up	down
MW0170020	Xanthosine	Nucleotide and Its metabolites	$C_{10}H_{12}N_4O_6$	1.87	1.62	0.04	up	down
MW0057544	PC (22:4(7Z,10Z,13Z,16Z)/15:0)	GP	$C_{45}H_{82}NO_8P$	6.59	1.51	0.01	up	up
MEDN0445	Orotidine	CoEnzyme and vitamins	$C_{10}H_{12}N_2O_8$	0.76	1.44	0.00	up	down
MW0110970	Cyclophosphamide	Alcohol and amines	$C_7H_{15}Cl_2N_2O_2P$	3.56	1.52	0.01	up	-
MW0002708	2-Aminoethyl diphenylborinate	Benzene and substituted derivatives	$C_{14}H_{16}BNO$	5.49	1.50	0.01	up	down
MW0143133	3-Vinylcatechol	Benzene and substituted derivatives	$C_8H_8O_2$	9.08	1.46	0.03	up	-
MW0139250	p-Coumaraldehyde	Benzene and substituted derivatives	$C_9H_8O_2$	3.85	1.54	0.03	up	-

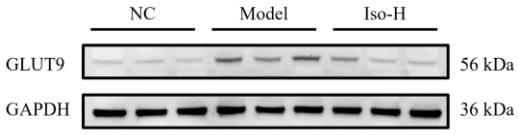
Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MW0009644	Didemethylcitalopram	Benzene and substituted derivatives	$C_{18}H_{17}FN_2O$	2.05	1.61	0.05	up	-
MEDN0075	N-Acetyl-L-phenylalanine	Amino acid and Its metabolites	$C_{11}H_{13}NO_3$	3.85	1.58	0.03	up	-
MEDP0082	S-Sulfo-L-Cysteine	Amino acid and Its metabolites	$C_3H_7NO_5S_2$	0.74	1.63	0.01	up	down
MW0108608	Spaglumic acid	Amino acid and Its metabolites	$C_{11}H_{16}N_2O_8$	2.23	1.51	0.04	up	-
MW0152190	Dihydrobiopterin	Heterocyclic compounds	$C_9H_{13}N_5O_3$	1.47	1.61	0.03	down	-
MW0169873	Spirilloxanthin	Terpenoids	$C_{42}H_{60}O_2$	7.98	1.54	0.01	down	-
MW0114733	L-Gulose	Carbohydrates and Its metabolites	$C_6H_{12}O_6$	0.79	1.50	0.05	down	-
MW0103352	2'-Deoxyuridine 5'-monophosphate	Nucleotide and Its metabolites	$C_9H_{13}N_2O_8P$	1.31	1.40	0.05	down	-
MW0159913	Inosine	Nucleotide and Its metabolites	$C_{10}H_{12}N_4O_5$	1.74	1.65	0.01	down	up
MW0012825	1-O-Hexadecyl-sn-glycero-3-phosphocholine	GP	$C_{24}H_{52}NO_6P$	8.81	1.51	0.00	down	-
MW0057056	PC (18:2(9Z,12Z)/18:3(6Z,9Z,12Z))	GP	$C_{44}H_{78}NO_8P$	8.75	1.67	0.01	down	-
MW0012968	1-hexadecanoyl-2-(9Z,12Z-octadecadienoyl)-sn-glycero-3-phosphocholine	GP	$C_{42}H_{80}NO_8P$	8.77	1.40	0.05	down	-
MW0057055	1,2-Dilinoleoyl-SN-glycero-3-phosphocholine	GP	$C_{44}H_{80}NO_8P$	7.32	1.45	0.03	down	-
MW0060403	PE-NMe2(18:2(9Z,12Z)/20:3(5Z,8Z,11Z))	GP	$C_{45}H_{80}NO_8P$	8.76	1.59	0.00	down	-

Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MEDP0638	LPE (16:1/0:0)	GP	$C_{21}H_{42}NO_7P$	6.65	1.47	0.05	down	-
MW0008586	Dimethylglycine	Amino acid and Its metabolites	$C_4H_9NO_2$	0.86	1.55	0.01	down	-
MW0122482	1-deoxy-1-(7-hydroxy-6-methyl-2,4-dioxo-3,4-dihydropteridin-8(2H)-yl)-D-ribitol	Heterocyclic compounds	$C_{12}H_{16}N_4O_7$	1.44	1.68	0.01	down	up
MW0128358	(R)-2-benzylsuccinic acid	Organic acid and Its derivatives	$C_{11}H_{12}O_4$	6.06	1.53	0.04	down	-
MEDN0202	α-Ketoglutaric Acid (α-KG)	Organic acid and Its derivatives	$C_5H_6O_5$	1.18	1.34	0.05	down	-
MW0115674	Chloroacetyl chloride	Aldehyde,Ketones,Esters	$C_2H_2Cl_2O$	0.68	1.55	0.02	down	-
MW0159977	9-[(4aR,6R,7R,7aS)-2,7-dihydroxy-2-oxo-4a,6,7,7a-tetrahydro-4H-furo[3,2-d][1,3,2]dioxaphosphinin-6-yl]-2-amino-3H-purin-6-one	Others	$C_{10}H_{12}N_5O_7P$	1.42	1.53	0.01	down	up
MEDL00630	Thyroxine	Hormones and hormone related compounds	$C_{15}H_{11}I_4NO_4$	5.32	1.41	0.03	down	-
MW0169017	Daidzein	Flavonoids	$C_{15}H_{10}O_4$	7.10	1.62	0.01	down	-
MW0103577	Guanosine	Nucleotide and Its metabolites	$C_{10}H_{13}N_5O_5$	1.48	1.46	0.01	down	-
MW0105438	Adenine	Nucleotide and Its metabolites	$C_5H_5N_5$	1.07	1.63	0.00	down	-
MW0103407	5'-phosphoribosyl-N-formylglycinamide	Nucleotide and Its metabolites	$C_8H_{15}N_2O_9P$	1.44	1.37	0.01	down	up
MW0012966	1-Palmitoyl-2-linoleoyl-sn-glycero-3-phosphate	GP	$C_{37}H_{69}O_8P$	6.82	1.33	0.04	down	up

Index	Compounds	*Class I*	Formula	RT (min)	VIP	P-value	Model vs NC	Iso-H vs Model
MW0113931	Amygdalin	Benzene and substituted derivatives	$C_{20}H_{27}NO_{11}$	4.08	1.50	0.03	down	-
MW0000560	2,4,5-Trichlorophenoxyacetic acid	Benzene and substituted derivatives	$C_8H_5Cl_3O_3$	9.31	1.47	0.02	down	up
MW0169647	Phenylacetylglutamine	Amino acid and Its metabolites	$C_{13}H_{16}N_2O_4$	2.45	1.50	0.02	down	-

GLUT9





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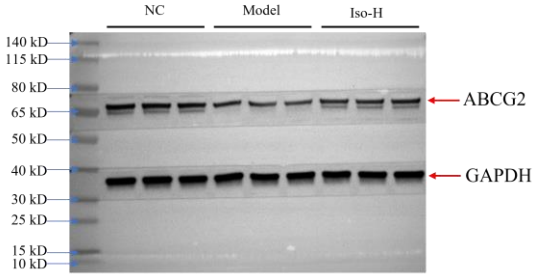

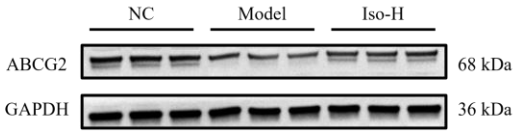

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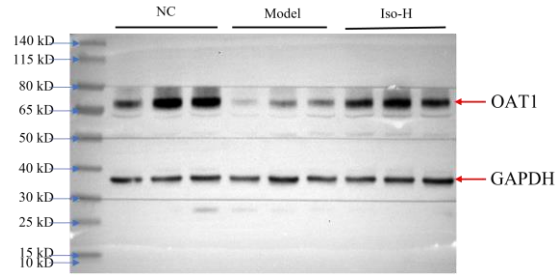

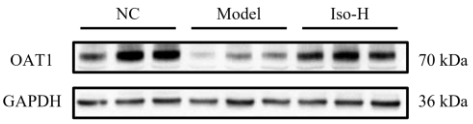

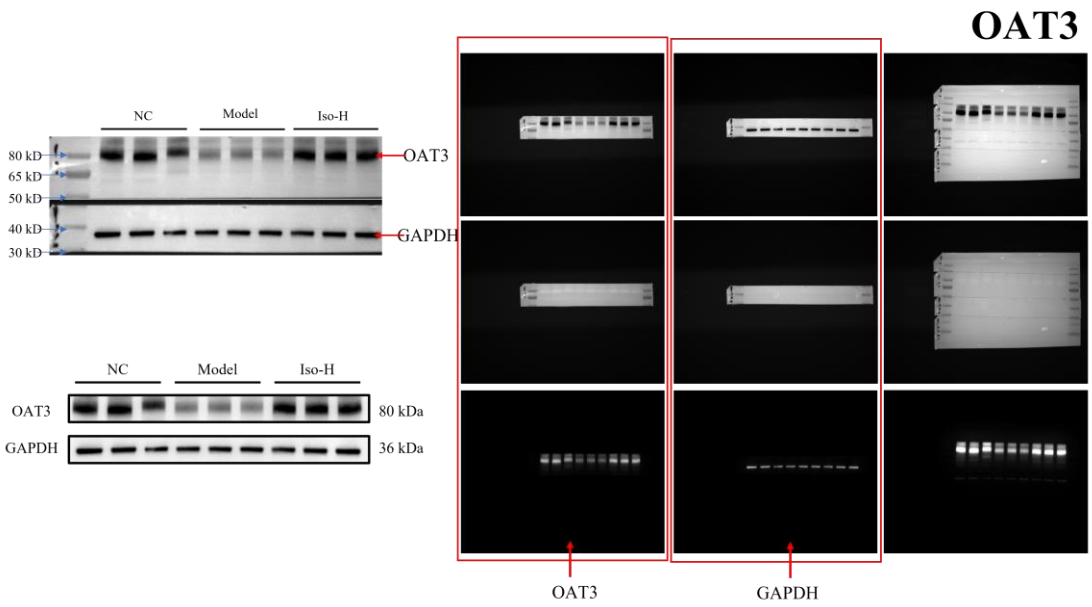
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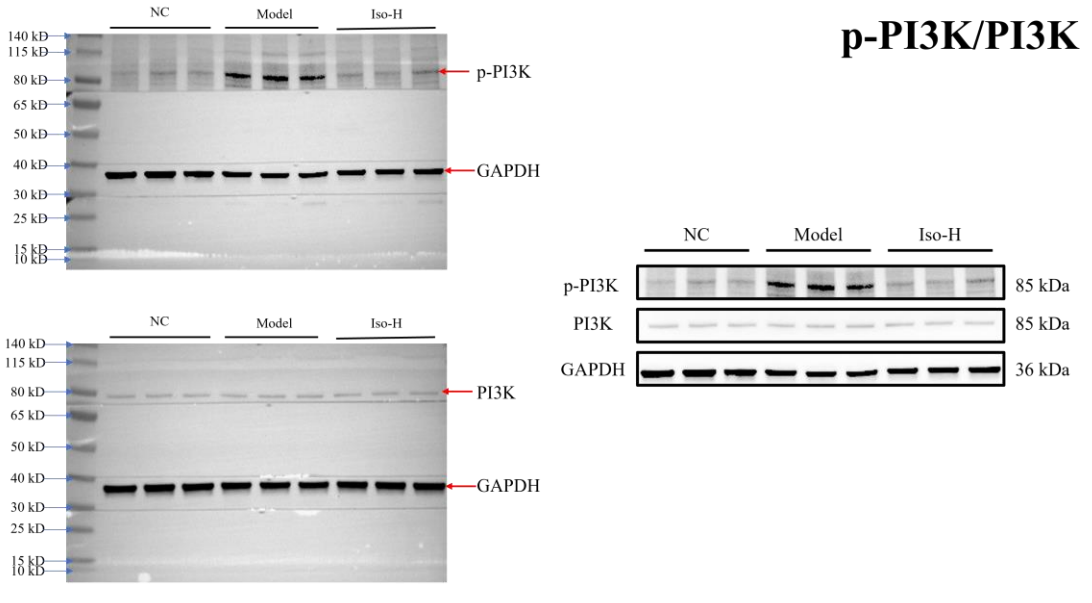
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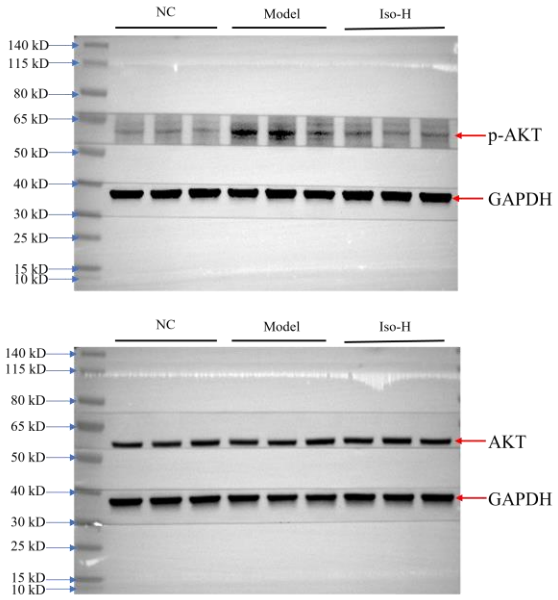

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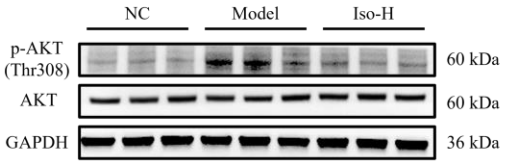

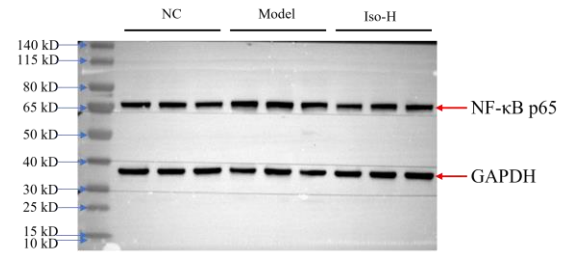

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